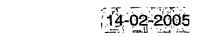
- 1. Use of a multifunctional angiotensin converting enzyme (ACE) inhibitor comprising in one molecule
 - i) an ACE-inhibitor component,
 - ii) at least one reactive oxygen species (ROS) scavenger component, not identical with said ACE-inhibitor component, and optionally
 - iii) at least one nitric oxide (NO) donor component, not identical with said ROS scavenger component

in the preparation of a medicament.

- 2. Use according to claim 1 of a multifunctional ACE inhibitor comprising
 - i) an ACE-inhibitor component,
 - ii) at least one ROS-scavenger component, not identical with said ACE-inhibitor component, and
 - iii) at least one nitric oxide (NO) donor component, not identical with said ROS scavenger component.
- Use according to claim 1, wherein said an ACE-inhibitor component is selected from the group consisting of compounds used in medicine as ACE-inhibitors, derivatives thereof, and compounds exhibiting affinity for ACE.
- 4. Use according to claim 1, wherein said ROS-scavenger component comprises an antioxidant reacting with ROS selected from the group consisting of superoxide, hydroxyl radicals, peroxynitrite, and hypochlorite.
- 5. Use according to claim 1, wherein said NO-donor comprises a group capable of providing nitric oxide in a form selected from uncharged and charged.
- 6. Use according to claim 4, wherein said ROS-scavenger component compriser a substituted N-oxide free radical.
- 7. Use according to claim 4, wherein the N-atom of said N-oxide is a member of a 3 to 7 membered heterocyclic ring.
- 8. Use according to claim 5, wherein said NO donor component comprises a group selected from —ONO₂, —ONO, —SNO, and —NONOate.



9. Use of a multifunctional ACE-inhibitor according to any one of claims 1 to 6 in the preparation of a medicament for treating or preventing a disorder selected from the group consisting of disorders in which treatment with an ACE-inhibitor is indicated, cardiovascular disorders, renal disorders, and diabetes associated disorders.

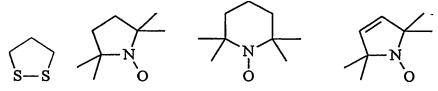
- 10. Use of a multifunctional ACE according to claim 1 in the preparation of a medicament for treating or preventing a disorder selected from the group consisting of ischaemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, cardiomyopathy, atherosclerosis, ischaemiareperfusion tissue injury, peripheral vascular disease, critical limb ischaemia, palpitations, arrhythmia, tachycardia, sinus. thyrotoxicosis, pheochromocytoma, tension, anxiety, alcohol withdrawal, anxiety, migraine, arterial aneurysm, microvascular diseases, hypertension selected from pulmonary-, systemic-, ocular-, obesity-, and pregnancy-induced, impotence, diabetes mellitus, hypercholestemia, Reaven's syndrome, diabetic nephropathy, insulin-resistance and glucose intolerance in diabetes, endothelial dysfunction or oxidative stress-induced diseases, drug or disease induced nephropathy, and esophageal varices.
- 11. Use according to claim 10, further preventing the occurrence of adverse effects of drugs, the development of tolerance to drugs, or the development of hypersensitivity to drugs.
- 12. Use according to claim 1, wherein said ACE inhibitor component is derived from an ACE inhibitor selected from the group consisting of Alacepril, Benazepril, Captopril, Ceronapril, Cilazapril, Delapril, Enalaprilat, Fosinopril, Imidapril Lisinopril, Moveltopril Perindopril, Quinapril, Ramipril, Spirapril, Temocapril, and Trandolapril.

13. Use according to claim 1, wherein said multifunctional ACE inhibitor has Formula I:

wherein R¹ may be selected from hydrogen (H), hydroxyl (OH), amino (NH₂), and alkoxy;

R² may be selected from H and lower alkyl;

R³ may be selected from -alkylene-Y and Y, wherein Y is a radical selected from the group consisting of:



R⁴ may be lower alkyl or H;

R⁵ may be selected from H, lower alkyl, -alkylene-Y or Y, wherein Y is a radical selected from the group consisting of:

or R⁴ and R⁵ may form a group selected from the formulae:

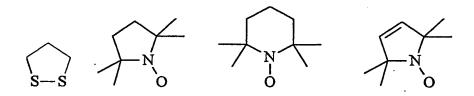
wherein X is selected from H, OH, SH, NH₂, ONO₂, SNO and NONOate.

14. Use according to claim 1, wherein said multifunctional ACE inhibitor has Formula II:

wherein R¹ may be selected from H, OH, NH₂, and alkoxy;

R² may be independently selected from SH, SNO;

R³ may be selected from -alkylene-Y and Y, wherein Y is a radical selected from the group consisting of:



R⁴ may be lower alkyl or H;

R⁵ may be selected from H, lower alkyl, -alkylene-Y and Y, wherein Y is a radical selected from the group consisting of:

or R⁴ and R⁵ may form a group selected from the formulae:

wherein X is selected from H, OH, SH, NH₂, ONO₂, SNO and NONOate; and

R⁶ may be lower alkyl.

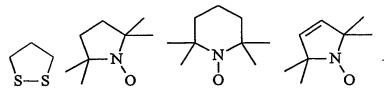
15. Use according to claim 1, wherein said multifunctional ACE inhibitor has Formula III:

wherein R¹ may be selected from OH, NH₂, alkoxy, and alkyl;

R² may be selected from OH, NH₂, alkoxy, and alkyl;

R³ is lower alkyl; and

R⁶ may be selected from -alkylene-Y and Y, wherein Y is a radical selected from the group consisting of:



X is (CH₂)_n; where n an integer from 0 to 5;

R⁴ is lower alkyl or H;

R⁵ may be selected from H, lower alkyl, -alkylene-Y, and Y, wherein Y is a radical selected from the group consisting of:

or R⁴ and R⁵ form a group independently selected from the formulae:

wherein X is selected from H, OH, SH, NH2, ONO2, SNO, and NONOate.

16. Use according to claim 1, wherein said multifunctional ACE inhibitor has Formula IV:

wherein m is an integer from 0 to 5;

- A and B are independently an optionally substituted saturated or unsaturated rings of from 4 to 18 atoms, wherein one or both comprise a ROS scavenger component; and wherein
- R^1 and R^5 are independently selected from H, optionally substituted lower alkyl, and $(CH_2)_nX$, where n is 0-2 and X is selected from OH, NH₂, SH, ONO, ONO₂, SNO and NONOate
- R² and R³ are independently selected from COR⁶ and (CH₂)_nX in which R⁶ is selected from OH, optionally substituted alkyl, optionally substituted acyl, optionally substituted aryl, optionally substituted heterocyclyl, and optionally substituted cycloalkyl, n is 0-2, and X is selected from OH, NH₂, SH, ONO, ONO₂, SNO, and NONOate;

R⁴ H or lower alkyl;

- A is an optionally substituted saturated or unsaturated ring system of from 4 to 18 atoms; and
- B is an optionally substituted, saturated or unsaturated ring system of from 4 to 18 atoms.

17. Use according to claim 16, wherein said ring A is selected from

and said ring B is selected from

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- 18. Use according to any one of claims 13 to 16, wherein said inhibitor comprises at least one ROS scavenger component being substituted N-oxide free radical in which the N-atom of said N-oxide is a member of 3 to 7 membered heterocyclic ring.
- 19. Use according to any one of claims 13 to 16, wherein said inhibitor comprises at least one NO-donor component selected from—ONO₂, —ONO, —SNO, and NONOate.
- 20. A multifunctional angiotensin converting enzyme (ACE) inhibitor comprising in one molecule
 - i) an ACE-inhibitor component,
 - ii) at least one reactive oxygen species (ROS) scavenger component, not identical with said ACE-inhibitor component, and optionally
 - iii) at least one nitric oxide (NO) donor component, not identical with said ROS scavenger component

for use as a medicament.

- 21. A method of treating or preventing a disorder selected from the group consisting of disorders in which treatment with an ACE-inhibitor is indicated, cardiovascular disorders, renal disorders, and diabetes associated disorders, in a mammal in need of said treating or preventing, comprising administering to said mammal an effective amount of a multifunctional ACE inhibitor comprising in one molecule i) an ACE inhibitor component, ii) at least one reactive oxygen species (ROS) scavenger component, and optionally iii) at least one nitric oxide (NO) donor component.
- 22. A method according to claim 21, wherein said disorder is selected from the group consisting of ischaemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, cardiomyopathy, atherosclerosis or Reaven's Syndrome, ischaemia-reperfusion tissue injury, peripheral vascular disease, critical limb ischaemia, palpitations, arrhythmias, arterial aneurysm, microvascular diseases, hypertension selected from pulmonary-, systemic-, ocular-, obesity-, and pregnancy-induced, impotence, diabetes mellitus,

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hypercholestemia, insulin-resistance and glucose intolerance in diabetes, endothelial dysfunction-induced diseases, drug or disease induced nephropathy, thyrotoxicosis, and migraine.

- 23. A method according to claim 21, wherein said administration or treatment is selected from the group consisting of topical, oral, and parenteral.
- 24. A method according to claim 21, wherein said administration or treatment is selected from the group consisting of suppository, by way of injection, and by way of infusion.
- 25. A method according to claim 21, wherein said multifunctional ACE inhibitor is administered by a route selected from intramuscular, intraperitoneal, intravenous, ICV, intracisternal injection or infusion, subcutaneous injection, implant, inhalation spray, nasal, vaginal, rectal, sublingual, and urethral.
- 26. A method according to claim 21, wherein said mammal is human.
- 27. A multifunctional ACE inhibitor comprising
 - i) an ACE-inhibitor component,
 - ii) at least one reactive oxygen species (ROS) scavenger component, not identical with said ACE-inhibitor component, and optionally
 - iii) at least one nitric oxide (NO) donor component, not identical with said ROS scavenger component
- 28. A multifunctional ACE inhibitor comprising
 - i) an ACE-inhibitor component,
 - ii) at least one reactive oxygen species (ROS) scavenger component, not identical with said ACE-inhibitor component, and
 - iii) at least one nitric oxide (NO) donor component, not identical with said ROS scavenger component.
- 29. A multifunctional ACE inhibitor according to claim 27, wherein said ACE-inhibitor component is selected from the group consisting of compounds used in medicine as ACE-inhibitors, derivatives thereof, and compounds exhibiting affinity for ACE.

30. A multifunctional ACE inhibitor according to claim 27, wherein said ROS-scavenger component comprises an antioxidant reacting with ROS selected from the group consisting of superoxide, hydroxyl radicals, peroxynitrite, and hypochlorite.

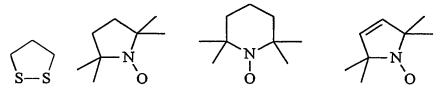
- 31. A multifunctional ACE inhibitor according to claim 27, wherein said ROS-scavenger component comprises any of alkenyl group, aryl group, substituted aryl group, sulfhydryl, dithiol in oxidized or reduced form, and group that is converted *in vivo* into a sulfhydryl in its oxidized or reduced form.
- 32. A multifunctional ACE inhibitor according to claim 27, wherein said ROS-scavenger component comprises a substituted N-oxide free radical, or a substituted or unsubstituted lipoic acid moiety,
- 33. A multifunctional ACE inhibitor according to claim 27, wherein said ROS-scavenger component comprises N-oxide free radical, wherein the nitrogen of said N-oxide free radical is within a 3-, 4-, 5-, 6- or 7-membered ring, wherein the ring may be substituted or unsubstituted with straight or branched alkyl groups, alkoxy groups or groups capable of donating NO.
- 34. A multifunctional ACE inhibitor according to claim 27, wherein said NO-donor comprises a group capable of providing nitric oxide in a form selected from uncharged and charged.
- 35. A multifunctional ACE inhibitor according to claim 27, wherein said NO-donor component comprises a group selected from —ONO₂, —ONO, SNO, and —NONOate.
- 36. A multifunctional ACE inhibitor according to claim 27, wherein said ACE inhibitor component is derived from ACE inhibitor selected from the group consisting of Alacepril, Benazepril, Captopril, Ceronapril, Cilazapril, Delapril, Enalapril, Enalaprilat, Fosinopril, Imidapril Lisinopril, Moveltopril Perindopril, Quinapril, Ramipril, Spirapril, Temocapril, and Trandolapril.

37. A multifunctional ACE inhibitor according to claim 27 having Formula I:

wherein R¹ may be selected from H, OH, NH₂, and alkoxy;

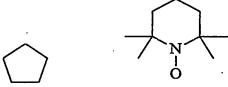
R² may be selected from H and lower alkyl;

R³ may be selected from -alkylene-Y and Y, wherein Y is a radical selected from the group consisting of:



R⁴ may be lower alkyl or H;

R⁵ may be selected from H, lower alkyl, -alkylene-Y or Y, wherein Y is a radical selected from the group consisting of:



or R⁴ and R⁵ may form a group selected from the formulae:

wherein X is selected from H, OH, SH, NH₂, ONO₂, SNO and NONOate.

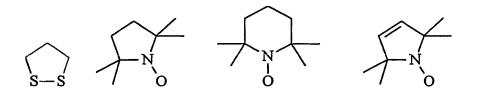
38. A multifunctional ACE inhibitor according to claim 37 wherein said R³ is selected from

39. A multifunctional ACE inhibitor according to claim 27 having Formula II:

wherein R¹ may be selected from H, OH, NH₂, and alkoxy;

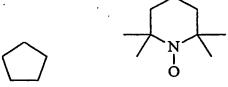
R² may be independently selected from SH, SNO;

R³ may be selected from -alkylene-Y and Y, wherein Y is a radical selected from the group consisting of:



R⁴ may be lower alkyl or H;

R⁵ may be selected from H, lower alkyl, -alkylene-Y and Y, wherein Y is a radical selected from the group consisting of:



or R⁴ and R⁵ may form a group selected from the formulae:

wherein X is selected from H, OH, SH, NH₂, ONO₂, SNO and NONOate; and

R⁶ may be lower alkyl.

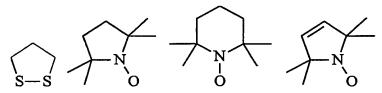
40. A multifunctional ACE inhibitor according to claim 27 having Formula III:

wherein R¹ may be selected from OH, NH₂, alkoxy, and alkyl;

R² may be selected from OH, NH₂, alkoxy, and alkyl;

R³ is lower alkyl; and

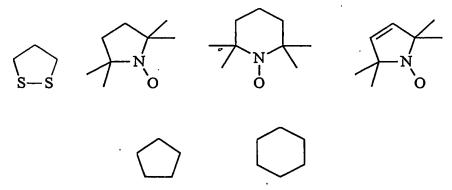
R⁶ may be selected from -alkylene-Y and Y, wherein Y is a radical selected from the group consisting of:



X is $(CH_2)_n$; where n an integer from 0 to 5;

R⁴ is lower alkyl or H;

R⁵ may be selected from H, lower alkyl, -alkylene-Y, and Y, wherein Y is a radical selected from the group consisting of:



or R⁴ and R⁵ form a group independently selected from the formulae:

wherein X is selected from H, OH, SH, NH₂, ONO₂, SNO, and NONOate.

41. A multifunctional ACE inhibitor according to claim 40 wherein said R⁶ is selected from

42. A multifunctional ACE inhibitor according to claim 27 having Formula IV:

wherein m is an integer from 0 to 5;

- A and B are independently an optionally substituted saturated or unsaturated rings of from 4 to 18 atoms, wherein one or both comprise a ROS scavenger component; and wherein
- R¹ and R⁵ are independently selected from H, optionally substituted lower alkyl, and (CH₂)_nX, where n is 0-2 and X is selected from OH, NH₂, SH, ONO, ONO₂, SNO and NONOate
- R² and R³ are independently selected from COR⁶ and (CH₂)_nX in which R⁶ is selected from OH, optionally substituted alkyl, optionally substituted acyl, optionally substituted aryl, optionally substituted heterocyclyl, and optionally substituted cycloalkyl, n is 0-2, and X is selected from OH, NH₂, SH, ONO, ONO₂, SNO, and NONOate;

R⁴ H or lower alkyl;

A is an optionally substituted saturated or unsaturated ring system of from 4 to 18 atoms; and

B is an optionally substituted, saturated or unsaturated ring system of from 4 to 18 atoms.

43. Use according to claim 42, wherein said ring A is selected from

and said ring B is selected from

- 44. A pharmaceutical composition comprising an inhibitor according to any one of claims 27 to 43, or a derivative thereof selected from the group consisting of optical isomer, solvate, and salt.
- 45. A pharmaceutical composition according to claim 44 further comprising a component selected from carrier, binding agent, stabilizer, adjuvant, diluent, excipient, surfactant, odorant, and a second pharmaceutically active agent.
- 46. A pharmaceutical composition according to claim 44, for use as a medicament for treating or preventing a disorder selected from the group consisting of disorders in which treatment with an ACE-inhibitor is indicated, cardiovascular disorders, renal disorders, and diabetes associated disorders.
- 47. A composition according to claim 44 for use as a medicament for treating a disorder selected from the group consisting of ischaemic heart disease, angina pectoris, myocardial infarction, congestive heart failure, cardiomyopathy, atherosclerosis or Reaven's Syndrome, ischaemia-reperfusion tissue injury, peripheral vascular disease, critical limb ischaemia, palpitations, arrhythmias, arterial aneurysm, microvascular diseases, hypertension selected from pulmonary-, systemic-, ocular-, obesity-, and pregnancy-induced, impotence, diabetes mellitus, hypercholestemia, insulin-resistance and glucose intolerance in diabetes, endothelial dysfunction-induced diseases, drug or disease induced nephropathy, thyrotoxicosis, and migraine.
- 48. A kit for administering a multifunctional ACE inhibitor comprising
 - a dosage amount of at least one compound having a component exhibiting ACE inhibitor activity and another component exhibiting ROS-scavenging activity,
 - ii) instructions for use, and

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iii) optionally means for the delivery of said compound.